Dr. Scott Masten
Office of Chemical Nomination and Selection
NIEHS/NTP
P.O. Box 12233
Research Triangle Park, NC 27709

September 19, 2001

Re: NIOSH's Draft Metal Working Fluids, Recommendation for Chronic Inhalation Study

Dear Dr. Masten:

The Independent Lubricant Manufacturers Association ("ILMA") appreciates this opportunity to provide additional comments to NIOSH on its Draft Metal Working Fluids, Recommendation for Chronic Inhalation Study ("Draft Recommendation"). ILMA's Safety, Health, Environmental and Regulatory Affairs Committee ("SHERA") prepared these comments.

As stated in our January 31, 2001 letter, ILMA continues to oppose NIOSH's recommendation to the National Toxicology Program ("NTP") for metal working fluid ("MWF") chronic inhalation studies. We maintain that MWFs are not appropriate candidates for chronic inhalation studies at this time. ILMA identified many specific comments in support of our position. One key reason for our position is that there are hundreds of MWF formulations and ingredients, allowing for an infinite number of combinations, making it nearly impossible for NIOSH to pick a representative formulation. Moreover, any study of virgin MWFS will not address in-use fluid changes, which may in fact be the largest contributing factor to any adverse health effects associated with occupational exposure to MWF formulations.

While ILMA believes that the proper selection of test materials is essential if NTP were to go forward with the Draft Recommendation, the Association cannot assist NTP in making such selections. We can find no common representative basis for selection.

To preserve the integrity of the scientific process, it is ILMA's position that NIOSH and NTP's deliberations must be free from any product-related influence by interested parties. Further, the complexity of MWFs and the competition in the MWF market complicate ILMA's ability to advise agencies in a product-neutral manner. Moreover, the Association does not posses product related information or data on MWF products, formulations, or analytical data. Therefore, participation would need to come directly from member companies.

ILMA strongly supports science that resolves the testing endpoint before initiating a testing program. The 1998 NIOSH Criteria Document, which was developed over several years and which included information and comments from interested third parties, including ILMA, states that current-day MWF formulations do not present a cancer risk, but rather a risk of *non-malignant chronic respiratory endpoints*. ILMA feels it is extremely important that the NTP not ignore this conclusion, regardless of the conclusions reached by the ICCEC.

ILMA members are committed to the safe use and handling of
Metal working fluids in the workplace. The Association welcomes the opportunity to support and participate in scientifically sound testing programs that advance workplace safety. I have attached ILMA's January 31, 2001 letter, which addresses other issues for NIOSH's consideration.

If you or other NIOSH staff members have any questions about either of these submissions, please contact Cathleen Barmoy, SHERA Committee Manager at 703/684-5574, ext. 121.

Sincerely,

Michael C. Metallo

Executive Director

cc/ILMA Board of Directors
SHERA Committee
Jeff Leiter, Collier Shannon Scott
Mark Torassen, NIOSH

January 31, 2001

Mr. Mark Torassen
National Institute for Occupational Safety and Health
Cincinnati, Ohio 45226

Re: November 14, 2000 Draft: Metal Working Fluids, Recommendation for Chronic Inhalation Study

Dear Mr. Torassen:

The Independent Lubricant Manufacturers Association ("ILMA") appreciates the opportunity to provide these comments to NIOSH on the Draft Metal Working Fluids Recommendation for Chronic Inhalation Study ("Draft Recommendation"). These comments are provided by the ILMA Health & Safety Task Force.

ILMA strongly opposes a NIOSH recommendation to the National Toxicology Program ("NTP") for Metal Working Fluid chronic inhalation studies. ILMA supports relevant and scientifically valid research on Metal Working Fluids (MWF), but cannot support this proposal. ILMA does not believe that MWF are an appropriate candidate for chronic inhalation NTP study at this time. ILMA believes that NIOSH's focus should be driven by its 1998 document: "Criteria for a Recommended Standard: Occupational Espouse to Metalworking Fluids" (Criteria Document), which states that current-day MWF formulations do not present a cancer risk, but rather, present a risk of non-malignant respiratory disease. Any NIOSH recommendation should thus focus on non-malignant chronic respiratory endpoints.

ILMA believes that NIOSH should delay any recommendation to NTP until the Environmental Protection Agency ("EPA") High Production Volume ("HPV") testing program is complete to determine whether any suspect components are identified. In the absence of additional data regarding MWF components, NIOSH does not have the ability to prioritize representative compositions for study and thus cannot sufficiently focus its testing recommendation.

ILMA offers specific comments in support of its opposition to the proposal:

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1. Cancer is not the greatest occupational health concern with the use of MWF.

2. None of the major chemicals used in MWF are suspect carcinogens.

3. There are too many different metalworking fluids commercially available for this approach to reach any definitive answers about the cancer risk of metalworking fluids.

4. Other information and programs in progress need to be reviewed to properly prioritize test subject for this approach.

5. MWFs are complex mixtures.

6. The NTP bioassay approach is an unproved tool for commercial mixtures.

A. MWF Should Not Be Addressed By NTP

1. Association Of Cancer To Occupational Use Of MWF Is Weak At Best
NIOSH, in 1998, published the document, "Criteria for a Recommended Standard: Occupational Exposure to Metalworking Fluids." NIOSH's recommendation for reducing MWF aerosol exposures is supported by what is said to be "substantial evidence associating some MWFs used before the mid-1970s with cancer at several organ sites" and NIOSH's continuing concern for the "potential for current MWF to pose a similar carcinogenic hazard." NIOSH also states, however, that the "primary basis of the NIOSH recommendation is the risk that MWF pose for nonmalignant respiratory disease (emphasis added). While there may be no actual test data on formulated products that show that current-day formulations do not pose any significant risk of cancer, there is certainly no evidence to suggest that the components of current-day formulations do pose a significant cancer risk. Thus we recommend NIOSH's principal focus in any recommendation be on non-malignant chronic respiratory endpoints and not be on cancer.

NIOSH states that there have been a small number of epidemiological studies that have adequate exposure characterization, and that the MWF constituent responsible for the site- specific cancer "remains to be determined." ILMA believes that none of the studies has adequate exposure characterization. Those studies that reported statistically significant effects found only very weak effects. None of the studies meet rigorously met criteria for establishing a cause-effect relationship.

Risk ratios of 1.2-5 are classes as weak. This range reported in those MWF studies with the strongest designed. Further, the larger the study size, the weaker the ratio risk. All studies should give the same result. The type of cancer supposedly found and the sub-group at risk varies with each study. Again, this is lacking in the published studies. Primary exposure to MWF is through skin absorption and inhalation. The only plausible carcinogens associated with MWF are the shale oil and nitrosamines. Use of nitrites in MWF began in about 1950. Excess liver cancer is not reported in the studies. Since 1976, nitrosamine levels in MWF have been reduced. (See discussion below).

2. Most Suspect Carcinogens Used In The Past Are No Longer Used In MWF
although a carcinogenic risk from the occupational use of MWF has not been

established, there have been many changes in commercial metalworking fluids over the last 50 years that would also serve to reduce carcinogenic risk.

Even though responsible companies began making strides to in the 1970s to make metalworking fluids safer, one cannot minimize the importance of the OSHA Hazard Communication standard (effective 1985) in altering the way chemicals are used in the workplace. This regulation, with especially strong provisions to assure label and MSDS statements for carcinogens contained at greater than 0.1% in a chemical product, created a strong incentive to provide chemical products for use in industrial and commercial operations that are as least hazardous as possible.

The purity of mineral oils has drastically improved over last few decades through great strides in refining technology. The carcinogenicity of mineral oils is a purity issue. Most toxicologists agree that carcinogenic activity is due to the presence of polynuclear aromatic and nitro aromatic impurities. A landmark was established in the understanding of the carcinogenicity issue with the IARC monograph in 1984. After a review of all the available data on mineral oil, IARC described criteria for the definition of a "severely refined mineral oil which did not seem to implicated as a carcinogen. OSHA quickly adopted this definition as guidance to the industry under the then new OSHA Hazard Communication Standard (29 C.F.R.§1910.1200). Responsible lubricant formulators reviewed their mineral oil specifications and have put processes into place to assure that only severely refined oils were used in MWFs and other lubricants.

Historically, nitrosamine contamination has been suspect as a possible source of cancer risk in MWF. Once it was discovered that the source of the nitrosamines was the use of inorganic nitrite salts as a rust preventative, responsible companies discontinued use of nitrites. EPA subsequently issued a rule under TSCA to prohibit the use of nitrites in MWF (40 C.F.R. § 721.4740). Since 1976, nitrosamine levels in MWF have been reduced from levels of parts-per-hundreds to parts-per-billion. Levels of nitrosodiethanolamine (NDLEA) in MWF are below the accepted de minimis level by three orders of magnitude.

Chlorinated paraffins have been another source of carcinogenic concern in MWF. Bioassays by the NTP have indicated that the activity is limited to short chain paraffin as opposed to longer chain paraffins. Again responsible formulators took early action to assure that only long chain-chlorinated paraffin's were used in MWF.

3. None Of The Major MWF Components In Use Today Are Suspect Carcinogens as explained below, MWF are complex mixtures manufactured by hundreds of small blenders. It is not known with certainty how many different MWFs are available in the marketplace nor how many different chemicals are used in MWFs. Recently ILMA members conducted a voluntary survey and approximately 100 chemicals were identified as being used in MWFs. It is believed these represent the major chemicals used to formulate MWFs. Toxicologists from ILMA member companies have examined the list and none of the chemicals are suspect carcinogens.

A number of comments can be made on these chemicals:

Mineral oil and chlorinated paraffins are more fully discussed in the section above. The data on diethanolamine and triethanolamine were recently reviewed by IARC and the expert body did not conclude that the evidence on

these chemicals warranted a carcinogenic classification. IARC has reviewed the existing data for DEA and TEA, including the NTP studies. (http://193.51.164.11/past&future/evaltab77.html) For DEA, they concluded that there was inadequate evidence in animals and classes DEA in group 3, cannot be classified as to its carcinogenicity in humans. For TEA, there was inadequate evidence for carcinogenicity in both humans and animals. TEA is also placed in class 3. MEA and TEA have been found to be non-sensitizers in human studies. They are widely and safely used in personal care products.

Many different fatty acids and fatty acid derivatives appear on the list. The scientific evidence indicates these chemicals are fairly innocuous and are not suspect structures for carcinogenicity.

Various alkyl alcohols and glycols (CAS 112-27-6, 107-21-1, 56-81-5, 107-41-5, 57-55-6) are also not suspect structures for carcinogenicity.

Several alkyl sulfides (CAS 68425-16-1, 68515-88-8, 72162-15-3) Alkylbenzene sulfonates (CAS 61789-86-4, 68608-26-4) are being voluntarily reviewed by individual companies or industry consortiums under the EPA HPV Chemical Testing Program. These chemicals are not mutagenic or genotoxic and there is no other data to indicate that they are suspect carcinogens.

4. Cancer Is Not The Top Health Concern Of Usage Of Modern MWF
NIOSH acknowledges that over the last several decades, the MWF industry has made substantial changes including changes in MWF composition and reduction in MWF impurities and exposure concentrations.

With respect to studies that have shown association between occupational exposure to MWF and asthma (Rosenman et al 1997b; Greaves et al 1995b; Eisen et al), these investigations conducting the UAW-GM studies did not consider semi-synthetics as a separate class, but regarded them as synthetic fluids. With the exception of one early study (Ely 1970), epidemiological studies of respiratory symptoms present generally consistent, and in the case of more recent studies, compelling epidemiological evidence indicating that occupational exposure to MWF aerosols has been associated symptoms that may be consistent with airway irritation, chronic bronchitis, and asthma. ILMA believes that these non-malignant respiratory effects should be the targets for research.

5. Many MWF Components Are In The EPA HPV Test Program And The Results Could Help NTP Prioritize. Approximately 2000 chemicals are being reviewed voluntarily under EPA HPV Program. Attachment 1 indicates which of the major metalworking components are being reviewed. Several are not being reviewed because of low concern or because they have gone through a similar review under the OECD SIDS Program.

Although it is believed that these chemicals are not suspect carcinogens, new data may be uncovered or generated during the HPV program. In view of the complexity of assessing hundreds of complex mixtures for carcinogenicity as explained below, new information from the HPV program may help prioritize the MWFs or the types of MWFs that should be examined for carcinogenicity. (Attachment 1)

6. Biocides Have Been Fully Evaluated By EPA
Biocides are required to be registered with EPA under FIFRA. Before

suing any biocides in a cancer bioassay, the data submitted to EPA should be reviewed to determine whether any biocides are suspect carcinogens.

B. Technical Difficulties In Using The NTP Approach To Study This Problem

1. MWF consist of 4 major types, straight oil, soluble oil, synthetic, semi-synthetic. Each type is represented by hundreds of complex mixtures of variable composition each of which consist of several of as many as 800 different components. MWFs differ widely by region and manufacturer. MWF composition may be changed by water properties in a region, like pH values, or by weather variations. In addition, MWF are routinely blended for a specific machine, material machined, and process. Signature MWF could exist for a day, a week, or a year, and then never be formulated or used again.

The MWF are shipped as a pure mixture. Once the container is opened and used, there are changes to the MWF as contaminants, some of which are microbial in nature, enter and grow in the MWF system. The MWF as received is thus a completely different mixture within hours, days, and weeks of use. The same MWF will exhibit microbial changes differently depending on the water properties, the cleanliness of the system, the purity of the air, the hygiene and housekeeping of the employees, the length of use, and the material being machined.

2. A Study Of Virgin Fluids Does Not Address In-Use Fluid Changes
A study of virgin fluids does not address the myriad of fluid changes that occur while the fluids are in use in a facility. When a MWF is charged into a sump, the composition is known. Unfortunately, this is true for only a short time. A number of chemical, physical and biological processes cause depletion or accumulation of individual components over time. A system typically loses 10% of its volume daily through evaporation of water. Replacing the lost water can reverse this, but this leads to an increase in the ionic strength of the mix as dissolved salts in the make up water build up.

Contamination of a fluid in use is inevitable. A comon source of contaminations are other lubricants used in other machinery such as hydraulic fluids and greases. This source of contamination is commonly caused "tramp oil." A system will occasionally have a higher content of tramp oil than of the primary metalworking fluid. These tramp oils are often formulated products themselves. They often introduce chemicals such as antioxidants, zinc dialkylthiophosphates and mercaptobenzothiazole into the fluid. Other common contaminants are cleaners, rust preventatives, degreasers, particulate and dissolved metals, dirt and anthropogenic wastes. As a rule of thumb, it can be assumed that any material present in a workplace will wind up in the fluid at some time.

Machining and grinding generate vast areas of nascent metal surface that are chemically reactive. Many fluid components, especially corrosion inhibitors, are stripped from the mix by these sites and are replaced by (largely unknown) reaction products. Many chemicals, especially biocides, are not stable at the pH levels commonly found in metalworking fluids. They decompose over time to form products that were not present in the original blend.

Fatty acids and monoethanolamine are known to be readily consumed by

mciroorganisms. Other chemicals, like mineral oil, may be degraded more slowly. The resulting metabolic products may be innocuous, like carbon dioxide, or irritating, like ammonia.

In soluble oils and semi-synthetics, the constituents can be present in the oil phase of the emulsion, in the water phase or both. As synthetic fluids become contaminated with tramp oil, the organic components will become distributed between the oil and the water. As the ionic strength of a used fluid increases with salt build up, organic molecules will be increasingly forced into the oil phase. As tramp oil is removed from the fluid, the more oil-soluble components will be depleted from the mix and their relative concentrations will decrease.

Even when this does not happen, the change in the oil-water distribution of an ingredient will make the effective dose of that ingredient in a used fluid different than the effective dose in a fresh fluid, at the same applied dose level.

Microbes are the contaminant of greatest concern from a health effects perspective. Animal models have shown that contaminated fluids have a greater irritation potential than fresh fluids. Anecdotal evidence from epidemiology studies has reported that fluids generate more complaints after several weeks of use. Respiratory problems and hypersensitivity pnuemonitis have been observed at very low exposure levels, in the presence of highly contaminated fluids. In many of these incidents, heavy contaminations of the ventilating systems as well as the metalworking fluid have been reported. In those cases, it is valid to ask if the fluid has contaminated the air system or vice versa.

The microbial population is not well defined. Historically, levels have based on counts of planktonic gram-negative bacteria on culture plates. Recent studies have shown that gram-negative bacteria may represent as little as 10% of the actual population in a fluid system. Further, the planktonic organisms are only a fraction of the total biomass present. Most of the population is present in huge masses of biofilm growing in the fluid, in splash areas or under machines.

The overall impact of microbial exposure is unknown and is an important area for future study. Any testing should be conducted to determine the magnitude of risk and should not involve the MWF as a chemical entity, but rather, as a vehicle for the microbial exposure.

3. NTP Cancer Bioassays Are Not The Proper Approach For Assessing Commercial Mixtures. The NTP bioassay has traditionally studied relatively pure single chemicals. Studying mixtures in a laboratory animal inhalation cancer bioassay presents a number of procedural and interpretative issues. Aerosols of mixtures may not be of uniform composition. Volatility of mixture components could add complexity to the exposure profile in the study. The analyte to determine exposure needs to be carefully chosen. Several analytes may be necessary to obtain a true picture of exposure. Any positive effects will cast a shadow of doubt on all components in the experimental mixture, which will not be able to be resolved until all the components can be tested separately. It will take a number of years to run these bioassays. If these results are inconclusive, simpler mixtures may need to be studied. This level of testing will also require an additional number of years. If the original effect is an anomalous effect due to the

animal species chosen, millions of dollars could be wasted on an effect that is not relevant to human health effects.

4. It May Be Difficult To Attain Aerosol Levels That Approach Maximum Tolerated Dose. ILMA members have conducted a number of studies on the acute inhalation toxicity of their products, as well as a few sub-acute studies. In acute studies, it has been impossible to achieve exposure levels high enough to cause acute effects after a one-hour exposure. The general practice has been to expose the animals for one hour at 200 mg/l and report the products as "non-toxic".

In 28-day studies, using exposure at 20 mg/l to a semi-synthetic fluid and a synthetic fluid, no toxic effects were observed in the exposed animals. A major obstacle to conducting inhalation studies has been the inability to achieve exposure levels high enough to cause toxic effects, even for a 28-day sub-acute study. Any choice of a small number of fluids to be tested would not result in a valid surrogate for all fluids.

Evaluation of a number of metalworking fluids by the mouse bioassay showed RD50 levels of 100-1000 mg/m3 for three hours exposure with the observation of sensory and pulmonary irritation. No significant differences were observed that could be attributed to differences in composition or fluid type. It seems reasonable to suspect that the over riding factor in this irritation is the alkaline nature of the fluids.

The maximum tolerated dose must be less than 100-1000 mg/m3 to avoid effects of pulmonary irritation. Since the epidemiological studies suggest that any carcinogenic effect must be very weak, it must be asked if these exposure levels would be high enough to give results that would be accepted if negative.

5. The Studies Cited By NIOSH Do Not Support the Proposal
The studies cited in the NIOSH Proposal do not provide compelling evidence that chronic, irreversible health hazards are caused by normal exposure to metalworking fluids. In every case, there is a degree of uncertainty, usually resulting from an experimental design that does not account for confounding factors. Authors suggest interpretations that cannot be ruled out but cannot be proven. A greater degree of appreciation of the complexity of the issues has resulted from the two symposia sponsored by American Automobile Manufacturers Association in 1995 and 1997. As a result, studies are now in progress or planning that will be more comprehensive and avoid some of these deficiencies. NIOSH, itself, under Dr. Vincent Castronova, has conducted a series of studies on the effects of dermal and inhalation exposure of animals to an unused semi-synthetic metalworking fluid. In a series of poster papers, they report no significant differences between control and exposed groups, unless the exposed animals have been impaired by sensitization with ovalbumin or fed diets deficient in Vitamins C and E. This work is continuing and promises to shed further light on the mechanisms of injury from metalworking fluid exposure.

C. Industry Studies May Yield Important New Information

The Metalworking Fluid Product Stewardship Group ("MWFPSG"), which is a subsidiary of ILMA, has initiated two studies that may yield information to facilitate NIOSH's efforts. The first study, which will be complete within the next 2 months, reviews the mammalian and in vitro toxicology of formulated MWF products.

The author of the report reviewed 180 company toxicology studies on 99 formulated MWF to create a compilation and evaluation of the mammalian and in vitro toxicology. The second project, which has just begun, will track and analyze the toxicological, chemical, and microbial changes in in-use fluid changes. Simultaneous health and mist exposure surveys of the workplace will allow identification of the root causes of any health effects found. The preliminary results of the second study should be available within a year.

It is reasonable to assume that other studies are also in progress and will lead to a better understanding of the extent and degree of health risks posed by metalworking fluids. Within a short time, there may be a better understanding of the risks of fluid exposure and the critical factors in avoiding those risks.

ILMA again urges NIOSH to reconsider its proposal and redirect its focus. ILMA looks forward to working with NIOSH on this important issue.

If you have questions about these comments, please call Dr. Richard Kraska, at (440) 943-1200 or Dr. John Howell, (630) 743-7340, of the ILMA Health & Safety Task Force.

Sincerely,

Michael C. Metallo
Executive Director

Enclosures
cc: ILMA Health & Safety Task Force
Stephanie Siegel, Collier Shannon Scott
Frank White, Organization Resources Counselors